ORIGINAL ARTICLE

Comparison of First Dose Hypotension with Captopril in Hypovolemic & Normovolemic Patients with Cardiac Failure

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ABSTRACT

The angiotensin converting enzyme inhibitors are the drugs of choice in congestive cardiac failure. The incidence of congestive cardiac failure is rising at the present times. Hundred patients with congestive cardiac failure either newly diagnosed or diagnosed already, but not on ACE therapy, admitted in Medical Units, Mayo Hospital, Lahore, were included in the study. Statistical analysis performed using SPSS 17.0. Results were expressed as mean ± SD. Each continuous parameter between the two groups, patients with hypovolemia/hyponatraemia and patients without hypovolemia/hyponatraemia analyzed with two tailed un-paired student's t-test. Congestive cardiac failure is a major problem and a common disease. The ACE inhibitors have become standard therapy for heart failure.

Key words: Hypotension, cardiac failure, hypovolemic & normovolemic

INTRODUCTION

The angiotensin converting enzyme inhibitors are the drugs of choice in congestive cardiac failure. The incidence of congestive cardiac failure is rising at the present times. The morbidity and mortality of heart failure patients is still high, even with the best techniques and management available. With the availability of drugs such as ACE inhibitors, it is now possible to antagonize the neurohormonal abnormalities caused by compensatory activation of renin angiotensin aldosterone system (RAS) and sympathetic nervous system stimulation (SNS) in patients with chronic heart failure. Clinical trials have shown that treatment regimens including these agents along with diuretics reduce the risk of deaths and hospitalization for worsening disease. Unfortunately, these drugs remain underused and frequently underdosed due to the fear of first dose hypotension, which is the most common side effect with these drugs especially captopril. This study was meant to know the incidence of first dose hypotension with ACE inhibitors (captopril) in patients with chronic heart failure (CHF).

PATIENTS & METHODS

Hundred patients with congestive cardiac failure either newly diagnosed or diagnosed already, but not on ACE therapy, admitted in Medical Units, Mayo Hospital, Lahore, were included in the study. Patients were divided into two groups, A and B. Group A consisted of patients which were normovolumic, not salt depleted and group B consisted of patients which were hyponatremic, volume depleted due to prior aggressive diuretic therapy. Control blood pressure readings were noted. Then test dose of captopril (6.25mg) was introduced. Blood pressure readings were noted at 30 minutes, 60 minutes and 90 minutes. First dose hypotension was observed by noting the drop in systolic blood pressure greater than 20 mmHg from the control systolic blood pressure reading after the peak effect of captopril (90 minutes) or drop in systolic blood pressure below 90 mmHg irrespective of the control reading. Patients having history of known hypersensitivity to ACE inhibitors and contraindicated for ACE inhibitors were excluded from the study.

RESULTS

Statistical analysis performed using SPSS 17.0. Results were expressed as mean ± SD. Each continuous parameter between the two groups, patients with hypovolemia/hyponatraemia and patients without hypovolemia/hyponatraemia analyzed with two tailed un-paired student's t-test. Categorical data examined using the chisquarec2 test. Out of 100 patients, first dose hypotension (FDH) was observed in 36 (36%) patients after 30 minutes, 40 (40%) patients after 60 minutes and 50 (50%) patients after 90 minutes. Out of 50 patients of group A, only 10 patients showed first dose hypotension and out of 50 patients of group B, 40 patients had first dose hypotension as shown in Table 1

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Table 1: Correlation between serum electrolyte levels and first dose hypotension (n=100)

		SBP Before Captopril Administration	Serum Electrolytes	Drop in SBP at 30 minutes	Drop in SBP at 60 minutes	Drop in SBP at 90 minutes
SBP before captopril administration	Pearson correlation Sig. (2 tailed)	1.000 NA***	-.321* .023	-.134 .353	.085 .556	-.336* .017
Serum electrolytes	Pearson correlation Sig. (2 tailed)	-.321* .023	1.000 NA***	.371** .008	.242 .091	.520** .000
Drop in SBP at 30 minutes	Pearson correlation Sig. (2 tailed)	-.134 .354	.371** .008	1.000 NA***	.551** .000	.536** .000
Drop in SBP at 60 minutes	Pearson correlation Sig. (2 tailed)	NA*** 	NA*** .091	.551** .000	1.000 NA***	.564** .000
Drop in SBP at 90 minutes	Pearson correlation Sig. (2 tailed)	-.336* .017	.520** .000	.536** .000	.564** .000	1.000 NA***

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed)
*** NA means not applicable

DISCUSSION

The aim of our study was to find out the percentage of patients with heart failure, who develop hypotension when ACE-inhibitor (captopril) was administered. A large number of patients with heart failure are admitted to medical units at Mayo Hospital and ACE-inhibitors are frequently prescribed as primary treatment usually without keeping in mind the major side effect first dose hypotension induced with these drugs. Another purpose of this study was to know the incidence of first dose hypotension in high-risk patients (Hyponatremic, volume depleted) and to compare it with normovolemic, not salt depleted patients.

Ischemic heart disease was the commonest cause of congestive cardiac failure in this study of 50 patients admitted in medical wards in Mayo Hospital, Lahore. It was similar to other studies, which show that in developing countries like Pakistan, ischemic heart disease is the leading cause of congestive cardiac failure[1,2,3].

In the 100 patients under study, 58 were male and 42 were female with a male to female ratio 1.4:1. This value was different as compared to another research [(4)] in West in which the overall ratio was 4:1. Out of 100 patients, 20 patients (20%) were diabetic. This was slightly more as compared to another study [(5)] in which the incidence of diabetes in CHF patients was 17%.

The dilated cardiomyopathy (DCM) of idiopathic origin was the second most common cause of CCF in this study. It was present in 40 patients (40%). In other studies the incidence of DCM was quite low being 21% and 5% in other researches[4,5]. It may be due to better investigative techniques in Western countries.

Hypertension was another common cause of CCF in this study, being present in 12 patients (12%). In another local study, prevalence was 5/1000. [(6,7)] Hypertensive heart failure is being commonest in another study in Hong Kong, [(8)] which is contrary to this study. Valvular heart disease was cause of CCF in 20 patients (20%) It shows that this disease is much common in Pakistan as contrary to other studies which show valvular heart disease as a cause of CCF in 15% [(6)], 13% [(4)] and 4%[9]. No case was recorded of high output states for example Anemia, hyperthyroidism etc as a cause of CCF in this study.

The diagnosis of CCF was made on history and clinical examination and was confirmed by ECG and Echocardiography. Echocardiography can detect ischemic/infracted myocardium, hypertrophy/dilatation of myocardium as well as valvular lesions. First dose hypotension was observed in 50 patients (50%) within first 90 minutes. It was similar to another study in which mean drop in BP greater than 20 mmHg after captopril administration was in about 50% of patients[10,11].

First dose hypotension occurred in 40 patients (40%) after 1 hour. It is slightly different from another study in which maximal BP fall occurred 1 hour after first dose of captopril (38%). [(12,13)] However, it is much contrary to another study in which first dose hypotension of captopril with in three hours was only 18%.[(14,15)] First dose hypotension was also observed in normotensives, normovolemic patients (10%). It was similar to another study, which showed this incidence about 15%[16].

First dose hypotension was much common in hyponatremic, volume depleted patients (40%) in this study. It was in accordance with another study, which said that FDH of captopril in sodium depleted patients was dependent on functional bradykinin B2 receptor[17,18,19,20]. First dose hypotension was much common in hypovolemic and hyponatremic patients (40%). It is in accordance with another study[19,21] which showed its incidence (38%).

First dose hypotension was less common in hypertensive patients (20%) in this study. It is similar to another study in which it was observed that first dose hypotension was less common in hypertensive patients. In other studies [22] high doses of ACE inhibitors (captopril, lisinopril) as compared to low doses were equally well tolerated. In this study low dose of captopril (6.25mg) caused first dose hypotension in only 10% of normovolemic, normotensive patients. It was not much contrary to other studies. The reason for this difference may be that in our setup usually higher doses are not given in trails so the effects of higher doses couldn't be evaluated. The fear of first dose hypotension prevents the doctors to prescribe ACE inhibitors in patients as observed in other study.[23] Therefore only 40% of CCF patients are treated with ACE inhibitors.

Also fear of first dose hypotension compels the doctors to under prescribe/under dose ACE inhibitors[24]. We also observed in our study that if hyponatremia corrected before administering captopril (group A), then ACE inhibitors (captopril) are well tolerated and blood pressure gets better even if it was low before. It was in accordance with other studies, which demonstrate that ACE inhibitors improve patients with low blood pressure[25]. Also some studies are in the favor of view that higher doses are better and well tolerated than lower doses[26,27,28].

We carried out this study with captopril keeping in mind the view that captopril is equally well tolerated and effective as compared to other ACE inhibitors like enalapril in treatment of CCF. It was similar to other studies[29,30] which show that captopril is equally better like other ACE inhibitors in tolerance and efficacy.

CONCLUSION

Congestive cardiac failure is a major problem and a common disease. The ACE inhibitors have become standard therapy for heart failure. Several trials e.g. CONSENSUS, SOLVD, SAVE, have established benefit of ACE inhibitor therapy in heart failure, however these drugs should be carefully introduced to patients with heart failure, because of risk of first dose hypotension. Heart failure patients are particularly prone to this phenomenon due to pre-existent hyper-reninemia and hyperaldosteronism. Captopril is the preferred agent for beginning, because of its predictable onset and short duration of action. Treatment is initiated with small test dose (6.25 mg) particularly in high-risk patients (patients on high diuretic therapy and hyponatremic). If diuretic is omitted at least 12-24 hours before introducing captopril and hyponatremia corrected before, then risk of first dose hypotension can be avoided sufficiently.

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